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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2	Dec 17	The CA Lexicon available in the CAPLUS and CA files
NEWS	3	Feb 06	Engineering Information Encompass files have new names
NEWS	4	Feb 16	TOXLINE no longer being updated
NEWS	5	Apr 23	Search Derwent WPINDEX by chemical structure
NEWS	6	Apr 23	PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
NEWS	7	May 07	DGENE Reload
NEWS	8	Jun 20	Published patent applications (A1) are now in USPATFULL
NEWS	9	JUL 13	New SDI alert frequency now available in Derwent's DWPI and DPCI

NEWS EXPRESS	July 11 CURRENT WINDOWS VERSION IS V6.0b, CURRENT MACINTOSH VERSION IS V5.0C (ENG) AND V5.0JB (JP), AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2001
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FILE 'HOME' ENTERED AT 11:41:45 ON 20 JUL 2001

=> file medline, uspat, hcaplus, embase, scisearch, dgene, wpids, frosti, fsta, cen, biotechds, biobusiness, ceaba

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.30	0.30

FILE 'MEDLINE' ENTERED AT 11:42:45 ON 20 JUL 2001

FILE 'USPATFULL' ENTERED AT 11:42:45 ON 20 JUL 2001

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FILE 'CEABA-VTB' ENTERED AT 11:42:45 ON 20 JUL 2001
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=> s cell proliferation

L1 283229 CELL PROLIFERATION

=> s l1 and (reversing?)

L2 788 L1 AND (REVERSING?)

=> s l2 and method

L3 554 L2 AND METHOD

=> s cell proliferation () reversal () method

L4 0 CELL PROLIFERATION (W) REVERSAL (W) METHOD

=> s cell proliferation adj reversing adj method

L5 0 CELL PROLIFERATION ADJ REVERSING ADJ METHOD

=> s l3 and activated blood cells

L6 0 L3 AND ACTIVATED BLOOD CELLS

=> s l3 and blood cells

L7 104 L3 AND BLOOD CELLS

=> s l7 and lactacystin

L8 0 L7 AND LACTACYSTIN

=> s lactacystin

L9 1899 LACTACYSTIN

=> s l9 and l7

L10 0 L9 AND L7

=> s l9 and rapamycin

L11 16 L9 AND RAPAMYCIN

=> s l11 and l7

L12 0 L11 AND L7

=> d l11 ti abs ibib tot

L11 ANSWER 1 OF 16 MEDLINE

TI Serine/threonine phosphorylation of IRS-1 triggers its degradation: possible regulation by tyrosine phosphorylation.

AB Insulin receptor substrate (IRS)-1 protein expression is markedly reduced in many insulin-resistant states, although the mechanism for this downregulation is unclear. In this study, we have investigated the early events in the insulin pathway that trigger the degradation of IRS-1. Incubation of the adipocytes with insulin induced a fast electrophoretic mobility shift of IRS-1 and a subsequent degradation of the protein. Wortmannin and **rapamycin** blocked this mobility shift of IRS-1, maintained the insulin-induced tyrosine phosphorylation of IRS-1, and blocked its degradation. In contrast, a glycogen synthase kinase 3 inhibitor, a mitogen-activated protein kinase/extracellular-regulated kinase inhibitor, and various protein kinase C inhibitors had no effect. Incubation with okadaic acid increased the serine/threonine phosphorylation of IRS-1 and its degradation, mimicking insulin, and its effect was prevented by the proteasome inhibitor **lactacystin**, as well as by **rapamycin**. Treatment of the cells with the tyrosine phosphatase inhibitor orthovanadate in the presence of insulin or okadaic acid partially inhibited the degradation of IRS-1. We propose that a **rapamycin**-dependent pathway participates as a negative regulator of IRS-1, increasing its serine/threonine phosphorylation, which triggers degradation. Thus, regulation of serine/threonine versus tyrosine phosphorylation may modulate IRS-1 degradation, affecting insulin sensitivity.

ACCESSION NUMBER: 2001092975 MEDLINE
DOCUMENT NUMBER: 21023282 PubMed ID: 11147790
TITLE: Serine/threonine phosphorylation of IRS-1 triggers its degradation: possible regulation by tyrosine phosphorylation.
AUTHOR: Pederson T M; Kramer D L; Rondinone C M
CORPORATE SOURCE: Diabetes Research, Pharmaceutical Products Division, Abbott
Laboratories, Abbott Park, Illinois 60064-3500, USA.
SOURCE: DIABETES, (2001 Jan) 50 (1) 24-31.
Journal code: E8X. ISSN: 0012-1797.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010125

L11 ANSWER 2 OF 16 MEDLINE

TI A **rapamycin**-sensitive pathway down-regulates insulin signaling via phosphorylation and proteasomal degradation of insulin receptor substrate-1.

AB Insulin receptor substrate-1 (IRS-1) is a major substrate of the insulin receptor and acts as a docking protein for Src homology 2 domain containing signaling molecules that mediate many of the pleiotropic actions of insulin. Insulin stimulation elicits serine/threonine phosphorylation of IRS-1, which produces a mobility shift on SDS-PAGE, followed by degradation of IRS-1 after prolonged stimulation. We investigated the molecular mechanisms and the functional consequences of these phenomena in 3T3-L1 adipocytes. PI 3-kinase inhibitors or **rapamycin**, but not the MEK inhibitor, blocked both the insulin-induced electrophoretic mobility shift and degradation of IRS-1. Adenovirus-mediated expression of a membrane-targeted form of the p110 subunit of phosphatidylinositol (PI) 3-kinase (p110CAAX) induced a mobility shift and degradation of IRS-1, both of which were inhibited by **rapamycin**. **Lactacystin**, a specific proteasome inhibitor, inhibited insulin-induced degradation of IRS-1 without any effect on its electrophoretic mobility. Inhibition of the mobility shift did not significantly affect tyrosine phosphorylation of IRS-1 or downstream insulin signaling. In contrast, blockade of IRS-1 degradation resulted in sustained activation of Akt, p70 S6 kinase, and mitogen-activated protein (MAP) kinase during prolonged insulin treatment. These results indicate that insulin-induced serine/threonine phosphorylation and degradation of IRS-1 are mediated by a **rapamycin**-sensitive pathway, which is downstream of PI 3-kinase and independent of ras/MAP kinase. The pathway leads to degradation of IRS-1 by the proteasome, which plays a major role in down-regulation of certain insulin actions during prolonged stimulation.

ACCESSION NUMBER: 2000474020 MEDLINE
DOCUMENT NUMBER: 20304194 PubMed ID: 10847581
TITLE: A **rapamycin**-sensitive pathway down-regulates insulin signaling via phosphorylation and proteasomal degradation of insulin receptor substrate-1.
AUTHOR: Haruta T; Uno T; Kawahara J; Takano A; Egawa K; Sharma P M;
Olefsky J M; Kobayashi M
CORPORATE SOURCE: First Department of Medicine, Toyama Medical and Pharmaceutical University Japan.. tharuta-tym@umin.ac.jp
CONTRACT NUMBER: DK-33651 (NIDDK)
SOURCE: MOLECULAR ENDOCRINOLOGY, (2000 Jun) 14 (6) 783-94.
Journal code: NGZ; 8801431. ISSN: 0888-8809.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001012
Last Updated on STN: 20001012
Entered Medline: 20001003

L11 ANSWER 3 OF 16 USPATFULL

TI Method for targeted degradation of intracellular proteins in vivo or ex vivo

AB A method for in vivo selective targeted degradation of intracellular proteins in situ by inducing in vivo or ex vivo in cells a production of
dual-function protein comprising N-terminal domain as well as a

C-terminal domain or delivering the dual-function protein. The N-terminal domain of the dual-function protein destabilizes the target protein and directs its degradation when linked to it through a linker between the target protein and between the protein agent of the invention. The protein degradation directing N-terminal domain is a subregion within the first 97 amino acids corresponding to the N-terminus of protein antizyme.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2001:55442 USPATFULL
TITLE:	Method for targeted degradation of intracellular proteins in vivo or ex vivo
INVENTOR(S):	Coffino, Philip, San Francisco, CA, United States Li, Xianqiang, Palo Alto, CA, United States
PATENT ASSIGNEE(S):	The Regents of the University of California, Oakland, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6217864	B1	20010417
APPLICATION INFO.:	US 1999-243273		19990202 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1996-603575, filed on 23 Feb 1996, now patented, Pat. No. US 5866121, issued on 2 Feb 1999		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Achutamurthy, Ponnathapu		
ASSISTANT EXAMINER:	Saidha, Tekchand		
LEGAL REPRESENTATIVE:	Verny, Hana		
NUMBER OF CLAIMS:	17		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	22 Drawing Figure(s); 9 Drawing Page(s)		
LINE COUNT:	2197		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2001 ACS

TI Serine/threonine phosphorylation of IRS-1 triggers its degradation: possible regulation by tyrosine phosphorylation

AB Insulin receptor substrate (IRS)-1 protein expression is markedly reduced in many insulin-resistant states, although the mechanism for this downregulation is unclear. In this study, the early events in the insulin pathway that trigger the degrdn. of IRS-1 were investigated. Incubation of the adipocytes with insulin induced a fast electrophoretic mobility shift of IRS-1 and a subsequent degrdn. of the protein. Wortmannin and **rapamycin** blocked this mobility shift of IRS-1, maintained the insulin-induced tyrosine phosphorylation of IRS-1, and blocked its degrdn.

In contrast, a glycogen synthase kinase 3 inhibitor, a mitogen-activated protein kinase/extracellular-regulated kinase inhibitor, and various protein kinase C inhibitors had no effect. Incubation with okadaic acid increased the serine/threonine phosphorylation of IRS-1 and its degrdn., mimicking insulin, and its effect was prevented by the proteasome inhibitor **lactacystin**, as well as by **rapamycin**.

Treatment of the cells with the tyrosine phosphatase inhibitor orthovanadate in the presence of insulin or okadaic acid partially inhibited the degrdn. of IRS-1. Thus, a **rapamycin**-dependent pathway participates as a neg. regulator of IRS-1, increasing its serine/threonine phosphorylation, which triggers degrdn. Thus, regulation of serine/threonine vs. tyrosine phosphorylation may modulate IRS-1 degrdn., affecting insulin sensitivity.

ACCESSION NUMBER:	2001:26737 HCAPLUS
DOCUMENT NUMBER:	134:220820

TITLE: Serine/threonine phosphorylation of IRS-1 triggers its degradation: possible regulation by tyrosine phosphorylation
AUTHOR(S): Pederson, Terry M.; Kramer, Deborah L.; Rondinone, Cristina M.
CORPORATE SOURCE: Diabetes Research, Pharmaceutical Products Division, Abbott Laboratories, Abbott Park, IL, 60064-3500, USA
SOURCE: Diabetes (2001), 50(1), 24-31
CODEN: DIAEAZ; ISSN: 0012-1797
PUBLISHER: American Diabetes Association
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 52
REFERENCE(S): (1) Anai, M; Diabetes 1998, V47, P13 HCAPLUS
(2) Araki, E; Nature 1994, V372, P186 HCAPLUS
(3) Caro, J; J Clin Invest 1986, V78, P249 HCAPLUS
(6) De Fea, K; J Biol Chem 1997, V272, P31400 HCAPLUS
(7) Eldar-Finkelman, H; Proc Natl Acad Sci U S A 1997, V94, P9660 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2001 ACS
TI A **rapamycin**-sensitive pathway down-regulates insulin signaling via phosphorylation and proteasomal degradation of insulin receptor substrate-1
AB Insulin receptor substrate-1 (IRS-1) is a major substrate of the insulin receptor and acts as a docking protein for Src homol. 2 domain contg. signaling mols. that mediate many of the pleiotropic actions of insulin. Insulin stimulation elicits serine/threonine phosphorylation of IRS-1, which produces a mobility shift on SDS-PAGE, followed by degrdn. of IRS-1 after prolonged stimulation. The authors investigated the mol. mechanisms and the functional consequences of these phenomena in 3T3-L1 adipocytes. PI 3-kinase inhibitors or **rapamycin**, but not the MEK inhibitor, blocked both the insulin-induced electrophoretic mobility shift and degrdn. of IRS-1. Adenovirus-mediated expression of a membrane-targeted form of the p110 subunit of phosphatidylinositol (PI) 3-kinase (p110CAAX) induced a mobility shift and degrdn. of IRS-1, both of which were inhibited by **rapamycin**. **Lactacystin**, a specific proteasome inhibitor, inhibited insulin-induced degrdn. of IRS-1 without any effect on its electrophoretic mobility. Inhibition of the mobility shift did not significantly affect tyrosine phosphorylation of IRS-1 or downstream insulin signaling. In contrast, blockade of IRS-1 degrdn. resulted in sustained activation of Akt, p70 S6 kinase, and mitogen-activated protein (MAP) kinase during prolonged insulin treatment. These results indicate that insulin-induced serine/threonine phosphorylation and degrdn. of IRS-1 are mediated by a **rapamycin** -sensitive pathway, which is downstream of PI 3-kinase and independent of ras/MAP kinase. The pathway leads to degrdn. of IRS-1 by the proteasome, which plays a major role in down-regulation of certain insulin actions during prolonged stimulation.
ACCESSION NUMBER: 2000:521341 HCAPLUS
DOCUMENT NUMBER: 133:188242
TITLE: A **rapamycin**-sensitive pathway down-regulates insulin signaling via phosphorylation and proteasomal degradation of insulin receptor substrate-1
AUTHOR(S): Haruta, Tetsuro; Uno, Tatsuhito; Kawahara, Junko; Takano, Atsuko; Egawa, Katsuya; Sharma, Prem M.; Olefsky, Jerrold M.; Kobayashi, Masashi
CORPORATE SOURCE: First Department of Medicine, Toyama Medical and Pharmaceutical University, Toyama, 930-0194, Japan

SOURCE: Mol. Endocrinol. (2000), 14(6), 783-794
CODEN: MOENEN; ISSN: 0888-8809
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 48
REFERENCE(S):
(1) Baumeister, W; Cell 1998, V92, P367 HCAPLUS
(2) Brown, E; Nature 1995, V377, P441 HCAPLUS
(3) Cheatham, B; Endocr Rev 1995, V16, P117 HCAPLUS
(4) Chin, J; J Biol Chem 1993, V268, P6338 HCAPLUS
(5) Chin, J; Mol Endocrinol 1994, V8, P51 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2001 ACS
TI The use of proteasome inhibitors for treating cancer, inflammation, autoimmune disease, graft rejection and septic shock, and screening method
AB The present invention relates to compns. comprising proteasome inhibitors, such as lactocystin and analogs thereof. These compns. are used for the following purposes: (1) to disrupt mitochondrial function (useful against cancer, inflammation, adverse immune reaction and hyperthyroidism), (2) to disrupt nitric oxide synthesis (useful against inflammation and septic shock), and (3) to reverse ongoing adverse immune reactions, such as autoimmune diseases and graft rejection. In the latter case, the compns. are administered once the patient's T cells are mostly activated. Proteasome inhibitors can also be combined with immunosuppressive drugs, e.g. **rapamycin**, cyclosporin A, and FK506. Finally, a method for screening a compd. having a proteasome inhibition activity is also disclosed and claimed.
ACCESSION NUMBER: 1999:311103 HCAPLUS
DOCUMENT NUMBER: 130:332911
TITLE: The use of proteasome inhibitors for treating cancer, inflammation, autoimmune disease, graft rejection and septic shock, and screening method
INVENTOR(S): Wu, Jiangping; Wang, Xin
PATENT ASSIGNEE(S): Centre de Recherche du Centre Hospitalier de l'Universite de Montreal, Can.
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9922729	A1	19990514	WO 1998-CA1010	19981029
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9897318	A1	19990524	AU 1998-97318	19981029
EP 967976	A1	20000105	EP 1998-951135	19981029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001508465	T2	20010626	JP 1999-525054	19981029

PRIORITY APPLN. INFO.: CA 1997-2219867 A 19971031
WO 1998-CA1010 W 19981029

REFERENCE COUNT: 15
REFERENCE(S):
(1) Conner, E; JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS 1997, V282(3), P1615 HCAPLUS
(2) Cui, H; PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA 1997, V94(14), P7515 HCAPLUS
(3) Griscavage, J; PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA 1996, V93(8), P3308 HCAPLUS
(4) Harvard College; WO 9417816 A 1994 HCAPLUS
(5) Harvard College; WO 9632105 A 1996 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2001 ACS
TI Cell cycle inhibitors
AB A review, with 46 refs., of the chem. and pharmacol. of the cell cycle inhibitors **rapamycin**, trichostatin, trapoxin A, and **lactacystin**.
ACCESSION NUMBER: 1998:166323 HCAPLUS
DOCUMENT NUMBER: 128:200453
TITLE: Cell cycle inhibitors
AUTHOR(S): Yoshida, Minoru
CORPORATE SOURCE: Grad. Sch. Agrobiol., Univ. Tokyo, Japan
SOURCE: Ketsueki, Men'eki, Shuyo (1996), 1(2), 184-191
CODEN: KMSHF6; ISSN: 1341-5824
PUBLISHER: Medikaru Rebyusha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

L11 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2001 ACS
TI Cell cycle inhibitors produced by microorganisms. The molecular mechanism of action
AB A review with 29 refs. on the mol. mechanism of action of cell cycle inhibitors produced by microorganisms, including radicicol, **rapamycin**, trichostin, tapoxin, and **lactacystin**.
ACCESSION NUMBER: 1996:239033 HCAPLUS
DOCUMENT NUMBER: 124:306195
TITLE: Cell cycle inhibitors produced by microorganisms. The molecular mechanism of action
AUTHOR(S): Yoshida, Minoru
CORPORATE SOURCE: Dep. Biotechnol., Univ. Tokyo, Tokyo, 113, Japan
SOURCE: Baiosaiensu to Indasutori (1996), 54(3), 182-7
CODEN: BIDSE6; ISSN: 0914-8981
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

L11 ANSWER 9 OF 16 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
TI A **rapamycin**-sensitive pathway down-regulates insulin signaling via phosphorylation and proteasomal degradation of insulin receptor substrate-1.
AB Insulin receptor substrate-1 (IRS-1) is a major substrate of the insulin receptor and acts as a docking protein for Src homology 2 domain containing signaling molecules that mediate many of the pleiotropic actions of insulin. Insulin stimulation elicits serine/threonine phosphorylation of IRS-1, which produces a mobility shift on SDS-PAGE, followed by degradation of IRS-1 after prolonged stimulation. We investigated the molecular mechanisms and the functional consequences of these phenomena in 3T3-L1 adipocytes. PI 3-kinase inhibitors or **rapamycin**, but not the MEK inhibitor, blocked both the insulin-induced electrophoretic mobility shift and degradation of IRS-I. Adenovirus- mediated expression of a membrane-targeted form of the p110 subunit of phosphatidylinositol (PI) 3-kinase (p110(CAAX)) induced a

mobility shift and degradation of IRS-1, both of which were inhibited by **rapamycin**. **Lactacystin**, a specific proteasome inhibitor, inhibited insulin-induced degradation of IRS-1 without any effect on its electrophoretic mobility. Inhibition of the mobility shift did not significantly affect tyrosine phosphorylation of IRS-1 or downstream insulin signaling. In contrast, blockade of IRS-1 degradation resulted in sustained activation of Akt, p70 S6 kinase, and mitogen-activated protein (MAP) kinase during prolonged insulin treatment. These results indicate that insulin-induced serine/threonine phosphorylation and degradation of IRS-1 are mediated by a **rapamycin**-sensitive pathway, which is downstream of PI 3-kinase and independent of ras/MAP kinase. The pathway leads to degradation of IRS-1 by the proteasome, which plays a major role in down-regulation of certain insulin actions during prolonged stimulation.

ACCESSION NUMBER: 2001126792 EMBASE
TITLE: A **rapamycin**-sensitive pathway down-regulates insulin signaling via phosphorylation and proteasomal degradation of insulin receptor substrate-1.
AUTHOR: Haruta T.; Uno T.; Kawahara J.; Takano A.; Egawa K.; Sharma P.M.; Olefsky J.M.; Kobayashi M.
CORPORATE SOURCE: T. Haruta, First Department of Medicine, Toyama Medical/Pharmaceutical Univ., 2630 Sugitani, Toyama 930-0194, Japan. tharuta-tym@umin.ac.jp
SOURCE: Molecular Endocrinology, (2000) 14/6 (783-794). Refs: 48 ISSN: 0888-8809 CODEN: MOENEN
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
LANGUAGE: English
SUMMARY LANGUAGE: English

L11 ANSWER 10 OF 16 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
TI Serine/threonine phosphorylation of IRS-1 triggers its degradation: Possible regulation by tyrosine phosphorylation.
AB Insulin receptor substrate (IRS)-1 protein expression is markedly reduced in many insulin-resistant states, although the mechanism for this downregulation is unclear. In this study, we have investigated the early events in the insulin pathway that trigger the degradation of IRS-1. Incubation of the adipocytes with insulin induced a fast electrophoretic mobility shift of IRS-1 and a subsequent degradation of the protein. Wortmannin and **rapamycin** blocked this mobility shift of IRS-1, maintained the insulin-induced tyrosine phosphorylation of IRS-1, and blocked its degradation. In contrast, a glycogen synthase kinase 3 inhibitor, a mitogen-activated protein kinase/extracellular-regulated kinase inhibitor, and various protein kinase C inhibitors had no effect. Incubation with okadaic acid increased the serine/threonine phosphorylation of IRS-1 and its degradation, mimicking insulin, and its effect was prevented by the proteasome inhibitor **lactacystin**, as well as by **rapamycin**. Treatment of the cells with the tyrosine phosphatase inhibitor orthovanadate in the presence of insulin or okadaic acid partially inhibited the degradation of IRS-1. We propose that a **rapamycin**-dependent pathway participates as a negative regulator of IRS-1, increasing its serine/threonine phosphorylation, which triggers degradation. Thus, regulation of serine/threonine versus tyrosine phosphorylation may modulate IRS-1 degradation, affecting insulin sensitivity.

ACCESSION NUMBER: 2001020515 EMBASE
TITLE: Serine/threonine phosphorylation of IRS-1 triggers its degradation: Possible regulation by tyrosine phosphorylation.
AUTHOR: Pederson T.M.; Kramer D.L.; Rondinone C.M.
CORPORATE SOURCE: Dr. C.M. Rondinone, Diabetes Research, Pharmaceutical

Products Division, Abbott Laboratories, Abbott Park, IL 60[redacted]-3500, United States. cristina[redacted]ndinone@abbott.com
SOURCE: Diabetes, (2001) 50/1 (24-31).
Refs: 52
ISSN: 0012-1797 CODEN: DIAEAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
030 Pharmacology
LANGUAGE: English
SUMMARY LANGUAGE: English

L11 ANSWER 11 OF 16 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
TI Proteasome inhibition: A new strategy in cancer treatment.
AB The ubiquitin proteasome pathway is a highly conserved intracellular pathway for the degradation of proteins. Many of the short-lived regulatory proteins which govern cell division, growth, activation, signaling and transcription are substrates that are temporally degraded by the proteasome. In recent years, new and selective inhibitors of the proteasome have been employed in cell culture systems to examine the anti-tumor potential of these agents. This review covers the chemistry of selected proteasome inhibitors, possible mechanisms of action in cell culture and the in vivo examination of proteasome inhibitors in murine and human xenograft tumor models in mice. One inhibitor, PS-341, has recently entered Phase I clinical trials in cancer patients with advanced disease to further test the potential of this approach.
ACCESSION NUMBER: 2000171137 EMBASE
TITLE: Proteasome inhibition: A new strategy in cancer treatment.
AUTHOR: Adams J.; Palombella V.J.; Elliott P.J.
CORPORATE SOURCE: J. Adams, ProScript, Inc., 38 Sidney Street, Cambridge, MA 02139, United States
SOURCE: Investigational New Drugs, (2000) 18/2 (109-121).
Refs: 103
ISSN: 0167-6997 CODEN: INNDDK
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English

L11 ANSWER 12 OF 16 SCISEARCH COPYRIGHT 2001 ISI (R)
TI Serine/threonine phosphorylation of IRS-1 triggers its degradation - Possible regulation by tyrosine phosphorylation
AB Insulin receptor substrate (IRS)-1 protein expression is markedly reduced in many insulin-resistant states, although the mechanism for this downregulation is unclear. In this study, we have investigated the early events in the insulin pathway that trigger the degradation of IRS-1. Incubation of the adipocytes with insulin induced a fast electrophoretic mobility shift of IRS-1 and a subsequent degradation of the protein. Wortmannin and **rapamycin** blocked this mobility shift of IRS-1, maintained the insulin-induced tyrosine phosphorylation of IRS-1, and blocked its degradation. In contrast, a glycogen synthase kinase 3 inhibitor, a mitogen-activated protein kinase/extracellular-regulated kinase inhibitor, and various protein kinase C inhibitors had no effect. Incubation with okadaic acid increased the serine/threonine phosphorylation of IRS-1 and its degradation, mimicking insulin, and its

effect was prevented by the proteasome inhibitor **lactacystin**, as well as by **rapamycin**. Treatment of the cells with the tyrosine phosphatase inhibitor orthovanadate in the presence of insulin or okadaic acid partially inhibited the degradation of IRS-1. We propose that a **rapamycin**-dependent pathway participates as a negative regulator of IRS-1, increasing its serine/threonine phosphorylation, which triggers degradation. Thus, regulation of serine/ threonine versus tyrosine phosphorylation may modulate IRS-1 degradation, affecting insulin sensitivity.

ACCESSION NUMBER: 2001:35508 SCISEARCH
THE GENUINE ARTICLE: 386XZ
TITLE: Serine/threonine phosphorylation of IRS-1 triggers its degradation - Possible regulation by tyrosine phosphorylation
AUTHOR: Pederson T M; Kramer D L; Rondinone C M (Reprint)
CORPORATE SOURCE: Abbott Labs, Div Pharmaceut Prod, Diabet Res, Dept 47H, AP9A, Abbott Pk, IL 60064 USA (Reprint); Abbott Labs, Div Pharmaceut Prod, Diabet Res, Dept 47H, Abbott Pk, IL 60064
USA
COUNTRY OF AUTHOR: USA
SOURCE: DIABETES, (JAN 2001) Vol. 50, No. 1, pp. 24-31.
Publisher: AMER DIABETES ASSOC, 1660 DUKE ST, ALEXANDRIA, VA 22314 USA.
ISSN: 0012-1797.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 52
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L11 ANSWER 13 OF 16 SCISEARCH COPYRIGHT 2001 ISI (R)
TI A **rapamycin**-sensitive pathway down-regulates insulin signaling via phosphorylation and proteasomal degradation of insulin receptor substrate-1
AB Insulin receptor substrate-1 (IRS-1) is a major substrate of the insulin receptor and acts as a docking protein for Src homology 2 domain containing signaling molecules that mediate many of the pleiotropic actions of insulin, Insulin stimulation elicits serine/threonine phosphorylation of IRS-1, which produces a mobility shift on SDS-PAGE, followed by degradation of IRS-1 after prolonged stimulation. We investigated the molecular mechanisms and the functional consequences of these phenomena in 3T3-L1 adipocytes. PI 3-kinase inhibitors or **rapamycin**, but not the MEK inhibitor, blocked both the insulin-induced electrophoretic mobility shift and degradation of IRS-1. Adenovirus- mediated expression of a membrane-targeted form of the p110 subunit of phosphatidylinositol (PI) 3-kinase (p110(CAAX)) induced a mobility shift and degradation of IRS-1, both of which were inhibited by **rapamycin**. **Lactacystin**, a specific proteasome inhibitor, inhibited insulin-induced degradation of IRS-1 without any effect on its electrophoretic mobility. Inhibition of the mobility shift did not significantly affect tyrosine phosphorylation of IRS-1 or downstream insulin signaling. In contrast, blockade of IRS-1 degradation resulted in sustained activation of Akt, p70 S6 kinase, and mitogen-activated protein (MAP) kinase during prolonged insulin treatment. These results indicate that insulin-induced serine/threonine phosphorylation and degradation of IRS-1 are mediated by a **rapamycin**-sensitive pathway, which is downstream of PI 3-kinase and independent of ras/MAP kinase. The pathway leads to degradation of IRS-1 by the proteasome, which plays a major role in down-regulation of certain insulin actions during prolonged stimulation.

ACCESSION NUMBER: 2000:437512 SCISEARCH
THE GENUINE ARTICLE: 320ZN
TITLE: A **rapamycin**-sensitive pathway down-regulates insulin signaling via phosphorylation and proteasomal

degradation of insulin receptor substrate-1
AUTHOR: Ha[redacted]a T (Reprint); Uno T; Kawahara[redacted] Takano A; Egawa K; Sharma P M; Olefsky J M; Kobayashi M
CORPORATE SOURCE: TOYAMA MED & PHARMACEUT UNIV, DEPT MED 1, 2630 SUGITANI, TOYAMA 9300194, JAPAN (Reprint); UNIV CALIF SAN DIEGO, DEPT MED, DIV ENDOCRINOL & METAB, LA JOLLA, CA 92093; UNIV CALIF SAN DIEGO, WHITTIER INST DIABET, LA JOLLA, CA 92093; VET ADM RES SERV, LA JOLLA, CA 92161
COUNTRY OF AUTHOR: JAPAN; USA
SOURCE: MOLECULAR ENDOCRINOLOGY, (JUN 2000) Vol. 14, No. 6, pp. 783-794.
Publisher: ENDOCRINE SOC, 4350 EAST WEST HIGHWAY SUITE 500, BETHESDA, MD 20814-4110.
ISSN: 0888-8809.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 48
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L11 ANSWER 14 OF 16 SCISEARCH COPYRIGHT 2001 ISI (R)
TI The proteasome controls the expression of a proliferation-associated nuclear antigen Ki-67
AB The proteasome is a protease complex responsible for rapid, selective, and irreversible removal of regulatory proteins, as well as many other cellular proteins. In this study, we have demonstrated that a proliferation-associated nuclear protein Ki-67 depended on the proteasome for its rapid degradation. A proteasome-specific inhibitor **lactacystin** augmented Ki-67 protein levels in pancreatic cancer BxPC-3 cells while repressed the level of steady-state Ki-67 mRNA. Inhibition of the proteasome also led to accumulation of two CDK inhibitors p27(kip1) and p21(cip1) in the BxPC-3 cells. Failed reduction of Ki-67 protein and enhanced levels of the two CDK inhibitors are likely contributing factors for the suppressed BxPC-3 proliferation after proteasome inhibition. (C) 2000 Wiley-Liss, inc.
ACCESSION NUMBER: 2000:106842 SCISEARCH
THE GENUINE ARTICLE: 280KH
TITLE: The proteasome controls the expression of a proliferation-associated nuclear antigen Ki-67
AUTHOR: Wu Y L; Luo H Y; Kanaan N; Wu J P (Reprint)
CORPORATE SOURCE: UNIV MONTREAL, LAB TRANSPLANTAT IMMUNOL, RES CTR, CHUM, PAVIL DESEVE, ROOM Y-5616, NOTRE DAME CAMPUS, MONTREAL, PQ H2L 4M1, CANADA (Reprint); ZHEJIANG UNIV, ZHEJIANG MED COLL, AFFILIATED HOSP 2, DEPT SURG, HANGZHOU 310027, PEOPLES R CHINA; UNIV MONTREAL, NOTRE DAME HOSP, RES CTR, SERV NEPHROL, CHUM, MONTREAL, PQ H2L 4M1, CANADA; UNIV MONTREAL, NOTRE DAME HOSP, SERV NEPHROL, CHUM, MONTREAL, PQ H2L 4M1, CANADA; MCGILL UNIV, DEPT SURG, MONTREAL, PQ H3A 1A4, CANADA
COUNTRY OF AUTHOR: CANADA; PEOPLES R CHINA
SOURCE: JOURNAL OF CELLULAR BIOCHEMISTRY, (JAN 2000) Vol. 76, No. 4, pp. 596-604.
Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012.
ISSN: 0730-2312.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 29
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L11 ANSWER 15 OF 16 SCISEARCH COPYRIGHT 2001 ISI (R)
TI **Rapamycin** inhibits proteasome activator expression and proteasome activity
AB **Rapamycin** (RAPA) is a potent immunosuppressive drug, and certain of its direct or indirect targets might be of vital importance to the regulation of an immune response. In this study, we used differential hybridization to search for human genes whose expression was sensitive to RAPA. Seven RAPA-sensitive genes were found and one of them encoded a protein with high homology to the ct subunit of a proteasome activator (PA28 beta). This gene was later found to code for the IJ subunit of the proteasome activator (PA28 beta). Activated T and B cells had up-regulated PA28 beta expression at the mRNA level. Such up-regulation could be suppressed by RAPA, FK506, and cyclosporin A. RAPA and FK506 also repressed the up-regulated PA28 alpha messages in phytohemagglutinin (PHA) stimulated T cells. At the protein level, RAPA inhibited PA28 alpha and PA28 beta in the activated T cells according to immunoblotting and confocal microscopy. Probably as a consequence, there was a fourfold increase of proteasome activities in the peripheral blood mononuclear cell lysate after the PHA activation. RAPA could inhibit the enhanced part of the proteasome activity. Considering the critical role played by the proteasome in degrading regulatory proteins, our data suggest that the proteasome activator is a relevant and important downstream target of **rapamycin**, and that the immune response could be modulated through the activity of the proteasome.
ACCESSION NUMBER: 97:865944 SCISEARCH
THE GENUINE ARTICLE: YG422
TITLE: **Rapamycin** inhibits proteasome activator expression and proteasome activity
AUTHOR: Wang X; Omura S; Szweda L I; Yang Y; Berard J; Seminaro J;
Wu J P (Reprint)
CORPORATE SOURCE: UNIV MONTREAL, NOTRE DAME HOSP, LC SIMARD RES CTR, PAVIL DE SEVE Y-5616, 1560 SHERBROOKE ST E, MONTREAL, PQ H2L 4M1, CANADA (Reprint); UNIV MONTREAL, FAC MED, LOUIS CHARLES SIMARD RES CTR, LAB TRANSPLANTAT IMMUNOL, DEPT MED, MONTREAL, PQ H3C 3J7, CANADA; UNIV MONTREAL, FAC MED,
DEPT MED, SERV NEPHROL, MONTREAL, PQ H3C 3J7, CANADA; KITASATO INST, TOKYO 108, JAPAN; CASE WESTERN RESERVE UNIV, CLEVELAND, OH 44106; RW JOHNSON PHARMACEUT RES INST,
SAN DIEGO, CA 92121; UNIV SHERBROOKE, SHERBROOKE, PQ J1K 2R1, CANADA; MCGILL UNIV, DEPT SURG, MONTREAL, PQ H3A 2T5,
CANADA
COUNTRY OF AUTHOR: CANADA; JAPAN; USA
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (NOV 1997) Vol. 27, No. 11, pp. 2781-2786.
Publisher: VCH PUBLISHERS INC, 303 NW 12TH AVE, DEERFIELD BEACH, FL 33442-1788.
ISSN: 0014-2980.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 40
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L11 ANSWER 16 OF 16 SCISEARCH COPYRIGHT 2001 ISI (R)
TI Cyclosporine A is an uncompetitive inhibitor of proteasome activity and prevents NF-kappa B activation
AB Cyclosporine A is an immunosuppressive agent that is used clinically in

the prevention of transplant rejection and development of graft-versus-host disease. Recently, cyclosporine A has been shown to possess anti-inflammatory properties and is capable of inhibiting lipopolysaccharide-induced NF-kappa B activation, Ubiquitin-mediated proteasomal proteolysis plays a critical role in signal-induced NF-kappa B activation since it regulates both I kappa B degradation and p105 processing, it is also involved in the production of peptides for the assembly of MHC class I molecules. We report here that cylcosporine A acts as an uncompetitive inhibitor of the chymotrypsin-like activity of the 20S proteasome in vitro and that it suppresses lipopolysaccharide-induced I kappa B degradation and p105 processing in vivo demonstrating that inhibition of proteasome proteolysis is the mechanism by which cyclosporine A prevents NF-kappa B activation. A structurally unrelated immunosuppressant, **rapamycin**, did not inhibit the 20S proteasome in vitro. (C) 1997 Federation of European Biochemical Societies.

ACCESSION NUMBER: 97:641166 SCISEARCH
THE GENUINE ARTICLE: XT085
TITLE: Cyclosporine A is an uncompetitive inhibitor of proteasome activity and prevents NF-kappa B activation
AUTHOR: Meyer S; Kohler N G; Joly A (Reprint)
CORPORATE SOURCE: CV THERAPEUT INC, 3172 PORTER DR, PALO ALTO, CA 94304 (Reprint); CV THERAPEUT INC, PALO ALTO, CA 94304
COUNTRY OF AUTHOR: USA
SOURCE: FEBS LETTERS, (18 AUG 1997) Vol. 413, No. 2, pp. 354-358.
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
ISSN: 0014-5793.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 24
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

=> d his

(FILE 'HOME' ENTERED AT 11:41:45 ON 20 JUL 2001)

FILE 'MEDLINE, USPATFULL, HCAPLUS, EMBASE, SCISEARCH, DGENE, WPIDS, FROSTI, FSTA, CEN, BIOTECHDS, BIOBUSINESS, CEABA-VTB' ENTERED AT 11:42:45
ON 20 JUL 2001

L1	283229	S	CELL PROLIFERATION
L2	788	S	L1 AND (REVERSING?)
L3	554	S	L2 AND METHOD
L4	0	S	CELL PROLIFERATION () REVERSAL () METHOD
L5	0	S	CELL PROLIFERATION ADJ REVERSING ADJ METHOD
L6	0	S	L3 AND ACTIVATED BLOOD CELLS
L7	104	S	L3 AND BLOOD CELLS
L8	0	S	L7 AND LACTACYSTIN
L9	1899	S	LACTACYSTIN
L10	0	S	L9 AND L7
L11	16	S	L9 AND RAPAMYCIN
L12	0	S	L11 AND L7

=> d l7 ti abs ibib 1-11

L7 ANSWER 1 OF 104 USPATFULL

TI Prevention and treatment of cardiovascular pathologies

AB A **method** for treating or preventing cardiovascular pathologies by administering a compound of the formula (I): ##STR1##

wherein Z is C.dbd.O or a covalent bond; Y is H or O(C.sub.1 -C.sub.4)alkyl, R.sup.1 and R.sup.2 are individually (C.sub.1 -C.sub.4)allyl or together with N are a saturated heterocyclic group, R.sup.3 is ethyl or chloroethyl, R.sup.4 is H or together with R.sup.3 is --CH.sub.2 --CH.sub.2 -- or --S--, R.sup.5 is I, O(C.sub.1 -C.sub.4)alkyl or H and R.sup.6 is I, O(C.sub.1 -C.sub.4)alkyl or H with

the proviso that when R.sup.4 F R.sup.5, and R.sup.6 are H, R.sup.3 is not ethyl; or a pharmaceutically acceptable salt thereof, effective to activate or stimulate production of TGF-beta to treat and/or prevent conditions such as atherosclerosis, thrombosis, myocardial infarction, and stroke is provided. Useful compounds include idoxifene and salts thereof. Further provided is a **method** for identifying a compound that is a TGF-beta activator or production stimulator is provided. Another embodiment of the invention is an assay or kit to determine TGF-beta in vitro. Also provided is a therapeutic **method** comprising inhibiting smooth muscle **cell proliferation** associated with procedural vascular trauma employing the administration of tamoxifen or structural analogs thereof,

including compounds of formula (I).

ACCESSION NUMBER:	2001:112344 USPATFULL
TITLE:	Prevention and treatment of cardiovascular pathologies
INVENTOR(S):	Grainger, David J., Cambridge, United Kingdom Metcalfe, James C., Cambridge, United Kingdom Kunz, Lawrence L., Redmond, WA, United States Schroff, Robert W., Edmonds, WA, United States Weissberg, Peter L., Cambridge, United Kingdom
PATENT ASSIGNEE(S):	NeoRx Corporation, Seattle, WA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6262079	B1	20010717
APPLICATION INFO.:	US 1999-306606		19990506 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1998-82643, filed on 21 May

1998 Division of Ser. No. US 1995-486334, filed on 7 Jun 1995, now patented, Pat. No. US 5770609 Continuation-in-part of Ser. No. US 1994-242161, filed on 12 May 1994, now patented, Pat. No. US 5847007 Continuation-in-part of Ser. No. US 1993-61714, filed on 13 May 1993, now abandoned Continuation-in-part of Ser. No. US 1994-241844, filed on 12 May 1994, now abandoned Continuation-in-part of Ser. No. US 1993-62451, filed on 13 May 1993, now abandoned Continuation-in-part of Ser. No. US 1993-11669, filed on 28 Jan 1993, now abandoned Continuation-in-part of Ser. No. WO 1992-US8220, filed on 25 Sep 1992

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Henley, III, Raymond
LEGAL REPRESENTATIVE:	Schwegman, Lundberg, Woessner & Kluth, P.A.
NUMBER OF CLAIMS:	23
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT:	4234

L7 ANSWER 2 OF 104 USPATFULL
TI Surgical irrigation solution and **method** for inhibition of pain and inflammation
AB A **method** and solution for perioperatively inhibiting a variety of pain and inflammation processes at wounds from general surgical procedures including oral/dental procedures. The solution preferably includes multiple pain and inflammation inhibitory at dilute concentration in a physiologic carrier, such as saline or lactated Ringer's solution. The solution is applied by continuous irrigation of a wound during a surgical procedure for preemptive inhibition of pain and while avoiding undesirable side effects associated with oral, intramuscular, subcutaneous or intravenous application of larger doses of the agents. One preferred solution to inhibit pain and inflammation includes a serotonin.sub.2 antagonist, a serotonin.sub.3 antagonist, a histamine antagonist, a serotonin agonist, a cyclooxygenase inhibitor, a neurokinin.sub.1 antagonist, a neurokinin.sub.2 antagonist, a purinoceptor antagonist, an ATP-sensitive potassium channel opener, a calcium channel antagonist, a bradykinin.sub.1 antagonist, a bradykinin.sub.2 antagonist and a .mu.-opioid agonist.

ACCESSION NUMBER:	2001:111551 USPATFULL
TITLE:	Surgical irrigation solution and **method** for inhibition of pain and inflammation
INVENTOR(S):	Demopulos, Gregory A., Mercer Island, WA, United States Pierce, Pamela A., Tiburon, CA, United States Herz, Jeffrey M., Mill Creek, WA, United States
PATENT ASSIGNEE(S):	Omeros Medical Systems, Inc., Seattle, WA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6261279	B1	20010717
APPLICATION INFO.:	US 1998-72913		19980504 (9)

RELATED APPLN. INFO.:	Continuation of Ser. No. US 1996-670699, filed on 26 Jun 1996, now patented, Pat. No. US 5820583 Continuation-in-part of Ser. No. WO 1995-US16028, filed on 12 Dec 1995 Continuation-in-part of Ser. No. US 1994-353775, filed on 12 Dec 1994, now abandoned
DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Jarvis, William R. A.
LEGAL REPRESENTATIVE:	Christensen O'Connor Johnson Kindness PLLC
NUMBER OF CLAIMS:	18
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	16 Drawing Figure(s); 12 Drawing Page(s)
LINE COUNT:	3376

L7 ANSWER 3 OF 104 USPATFULL
TI Surgical irrigation solution and **method** for inhibition of pain and inflammation
AB A **method** and solution for perioperatively inhibiting a variety of pain and inflammation processes at wounds from general surgical procedures including oral/dental procedures. The solution preferably includes multiple pain and inflammation inhibitory at dilute concentration in a physiologic carrier, such as saline or lactated Ringer's solution. The solution is applied by continuous irrigation of a wound during a surgical procedure for preemptive inhibition of pain and while avoiding undesirable side effects associated with oral, intramuscular, subcutaneous or intravenous application of larger doses

of the agents. One preferred solution to inhibit pain and inflammation includes a serotonin.sub.2 antagonist, a serotonin.sub.3 antagonist, a histamine antagonist, a serotonin agonist, a cyclooxygenase inhibitor, a

neurokinin.sub.1 antagonist, a neurokinin.sub.2 antagonist, a purinoceptor antagonist, an ATP-sensitive potassium channel opener, a calcium channel antagonist, a bradykinin.sub.1 antagonist, a bradykinin.sub.2 antagonist and a .mu.-opioid agonist.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2001:102097 USPATFULL
TITLE:	Surgical irrigation solution and **method** for inhibition of pain and inflammation
INVENTOR(S):	Demopulos, Gregory A., Mercer Island, WA, United States
	Pierce, Pamela A., Tiburon, CA, United States
	Herz, Jeffrey M., Mill Creek, WA, United States
PATENT ASSIGNEE(S):	Omeros Medical Systems, Inc., Seattle, WA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6254585	B1	20010703
APPLICATION INFO.:	US 1998-109885		19980702 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1996-670699, filed on 26 Jun 1996, now patented, Pat. No. US 5820583 Continuation-in-part of Ser. No. WO 1995-US16028, filed on 12 Dec 1995 Continuation-in-part of Ser. No. US 1994-353775, filed on 12 Dec 1994, now abandoned

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Seidel, Richard K.
ASSISTANT EXAMINER:	Sirmons, Kevin C.
LEGAL REPRESENTATIVE:	O'Connor, ChristensenJohnson Kindness PLLC
NUMBER OF CLAIMS:	32
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	16 Drawing Figure(s); 12 Drawing Page(s)
LINE COUNT:	3284

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 4 OF 104 USPATFULL

TI Prevention and treatment of cardiovascular pathologies

AB A **method** for treating or preventing cardiovascular pathologies by administering a compound of the formula (I): ##STR1##

wherein Z is C.dbd.O or a covalent bond; Y is H or O(C.sub.1 -C.sub.4)alkyl, R.sup.1 and R.sup.2 are individually (C.sub.1 -C.sub.4)alkyl or together with N are a saturated heterocyclic group, R.sup.3 is ethyl or chloroethyl, R.sup.4 is H or together with R.sup.3 is --CH.sub.2 --CH.sub.2 -- or --S--, R.sup.5 is I, O(C.sub.1 -C.sub.4)alkyl or H and R.sup.6 is I, O(C.sub.1 -C.sub.4)alkyl or H with

the proviso that when R.sup.4, R.sup.5, and R.sup.6 are H, R.sup.3 is not ethyl; or a pharmaceutically acceptable salt thereof, effective to activate or stimulate production of TGF-beta to treat and/or prevent conditions such as atherosclerosis, thrombosis, myocardial infarction, and stroke is provided. Useful compounds include idoxifene and salts thereof. Further provided is a **method** for identifying a compound that is a TGF-beta activator or production stimulator is provided. Another embodiment of the invention is an assay or kit to determine TGF-beta in vitro. Also provided is a therapeutic **method** comprising inhibiting smooth muscle **cell proliferation** associated with procedural vascular trauma

employing the administration of tamoxifen or structural analogs thereof,
including compounds of formula (I).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2001:97942 USPATFULL
TITLE:	Prevention and treatment of cardiovascular pathologies
INVENTOR(S):	Grainger, David J., Cambridge, United Kingdom Metcalfe, James C., Cambridge, United Kingdom Weissberg, Peter L., Cambridge, United Kingdom
PATENT ASSIGNEE(S):	NeoRx Corporation, Seattle, WA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6251920	B1	20010626
APPLICATION INFO.:	US 1998-82643		19980521 (9)

RELATED APPLN. INFO.:	Division of Ser. No. US 1995-486334, filed on 7 Jun 1995, now patented, Pat. No. US 5770609 Continuation-in-part of Ser. No. US 1994-242161, filed on 12 May 1994, now patented, Pat. No. US 5847007 Continuation-in-part of Ser. No. US 1993-61714, filed on 13 May 1993, now abandoned Continuation-in-part of Ser. No. US 1994-241844, filed on 12 May 1994, now abandoned Continuation-in-part of Ser. No. US 1993-62451, filed on 13 May 1993, now abandoned Continuation-in-part of Ser. No. US 1993-11669, filed on 28 Jan 1993, now abandoned Continuation-in-part of Ser. No. WO 1992-US8220, filed on 25 Sep 1992, now abandoned
DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Henley, III, Patrick
LEGAL REPRESENTATIVE:	Schwegman, Lundberg, Woessner & Kluth, P.A.
NUMBER OF CLAIMS:	42
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT:	4366

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 5 OF 104 USPATFULL

TI Methods of inhibiting inflammation at the site of a central nervous system injury with alphaD-specific antibodies

AB Methods to inhibit inflammation and macrophage infiltration following spinal cord injury are disclosed along with methods to modulate TNF.alpha. release from cells expressing .alpha..sub.d are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2001:97420 USPATFULL
TITLE:	Methods of inhibiting inflammation at the site of a central nervous system injury with alphaD-specific antibodies
INVENTOR(S):	Gallatin, W. Michael, 8412 SE. 33rd Pl., Mercer Island, WA, United States 98040 Van der Vieren, Monica, 2446 NW. 64th St., Seattle, WA, United States 98107

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6251395	B1	20010626
APPLICATION INFO.:	US 1998-193043		19981116 (9)

RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1997-943363, filed

on 3 Oct 1997, now patented, Pat. No. US 5837478, issued on 17 Nov 1998 Continuation-in-part of Ser. No. US 1996-605672, filed on 22 Feb 1996, now patented, Pat. No. US 5817515, issued on 6 Oct 1998 Continuation-in-part of Ser. No. US 1994-362652, filed on 21 Dec 1994, now patented, Pat. No. US 5766850, issued on 16 Jun 1998 Continuation-in-part of Ser. No. US 1994-286889, filed on 5 Aug 1994, now patented, Pat. No. US 5470953, issued on 28 Nov 1995 Continuation-in-part of Ser. No. US 1993-173497, filed on 23 Dec 1993, now patented, Pat. No. US 5437958, issued on 1 Aug 1995

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Gambel, Phillip
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 6697
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 6 OF 104 USPATFULL

TI Surgical irrigation solution and **method** for inhibition of pain and inflammation

AB A **method** and solution for perioperatively inhibiting a variety of pain and inflammation processes at wounds from general surgical procedures including oral/dental procedures. The solution preferably includes multiple pain and inflammation inhibitory at dilute concentration in a physiologic carrier, such as saline or lactated Ringer's solution. The solution is applied by continuous irrigation of a wound during a surgical procedure for preemptive inhibition of pain and while avoiding undesirable side effects associated with oral, intramuscular, subcutaneous or intravenous application of larger doses of the agents. One preferred solution to inhibit pain and inflammation includes a serotonin.sub.2 antagonist, a serotonin.sub.3 antagonist, a histamine antagonist, a serotonin agonist, a cyclooxygenase inhibitor, a neurokinin.sub.1 antagonist, a neurokinin.sub.2 antagonist, a purinoceptor antagonist, an ATP-sensitive potassium channel opener, a calcium channel antagonist, a bradykinin.sub.1 antagonist, a bradykinin.sub.2 antagonist and a .mu.-opioid agonist.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2001:82772 USPATFULL
TITLE: Surgical irrigation solution and **method** for inhibition of pain and inflammation
INVENTOR(S): Demopulos, Gregory A., Mercer Island, WA, United States
Pierce, Pamela A., Tiburon, CA, United States
Herz, Jeffrey M., Mill Creek, WA, United States
PATENT ASSIGNEE(S): Omeros Medical Systems, Inc., Seattle, WA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6242447	B1	20010605
APPLICATION INFO.:	US 1998-72843		19980504 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1996-670699, filed on 26 Jun 1996, now patented, Pat. No. US 5820583 Continuation-in-part of Ser. No. WO 1995-US16028, filed on 12 Dec 1995 Continuation-in-part of Ser. No. US

1994-353775, filed on 12 Dec 1994, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Jarvis, William R. A.
LEGAL REPRESENTATIVE: Christensen O'Connor Johnson Kindness PLLC
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 16 Drawing Figure(s); 12 Drawing Page(s)
LINE COUNT: 3308
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 7 OF 104 USPATFULL
TI Multivalent ligands which modulate angiogenesis
AB Disclosed are novel multivalent ligands represented by the following structural formula: ##STR1##

B is a multilinker backbone.

n is an integer from two to about twenty.

Each L is a covalent bond or linking group.

Each P is a peptide having from about 10 to about 30 amino acid residues. At least two of the peptides P are a peptide derivative of an AHR of an angiogenic protein, a hybrid peptide, a peptide derivative of a hybrid peptide or a combination thereof. Each peptide and each linker or covalent bond is independently chosen. The disclosed multivalent ligands can be used to modulate angiogenesis in a mammal.

Also disclosed are novel peptide derivatives of an AHR of an angiogenic protein, novel hybrid peptides, peptide derivatives of the novel hybrid peptides and polypeptide multivalent ligands thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2001:75369 USPATFULL
TITLE: Multivalent ligands which modulate angiogenesis
INVENTOR(S): Ben-Sasson, Shmuel A., Jerusalem, Israel
PATENT ASSIGNEE(S): Children's Medical Center Corporation, Boston, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6235716	B1	20010522
APPLICATION INFO.:	US 1999-474743		19991229 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1998-46985, filed on 24 Mar 1998, now patented, Pat. No. US 6121236
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Davenport, Avis M.
LEGAL REPRESENTATIVE: Hamilton Brook Smith & Reynolds, P.C.
NUMBER OF CLAIMS: 60
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 15 Drawing Figure(s); 13 Drawing Page(s)
LINE COUNT: 1754
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 8 OF 104 USPATFULL
TI Surgical irrigation solution and **method** for inhibition of pain and inflammation
AB A **method** and solution for perioperatively inhibiting a variety of pain and inflammation processes at wounds from general surgical procedures including oral/dental procedures. The solution preferably includes multiple pain and inflammation inhibitory at dilute concentration in a physiologic carrier, such as saline or lactated

Ringer's solution. The solution is applied by continuous irrigation of a wound during a s[redacted]gical procedure for preemptive [redacted]ibition of pain and while avoiding undesirable side effects associated with oral, intramuscular, subcutaneous or intravenous application of larger doses of the agents. One preferred solution to inhibit pain and inflammation includes a serotonin.sub.2 antagonist, a serotonin.sub.3 antagonist, a histamine antagonist, a serotonin agonist, a cyclooxygenase inhibitor, a neurokinin.sub.1 antagonist, a neurokinin.sub.2 antagonist, a purinoceptor antagonist, an ATP-sensitive potassium channel opener, a calcium channel antagonist, a bradykinin.sub.1 antagonist, a bradykinin.sub.2 antagonist and a .mu.-opioid agonist.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2001:47271 USPATFULL
TITLE:	Surgical irrigation solution and **method** for inhibition of pain and inflammation
INVENTOR(S):	Demopulos, Gregory A., Mercer Island, WA, United States Pierce, Pamela A., Tiburon, CA, United States Herz, Jeffrey M., Mill Creek, WA, United States
PATENT ASSIGNEE(S):	Omeros Medical Systems, Inc., Seattle, WA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6210394	B1	20010403
APPLICATION INFO.:	US 1998-177671		19981022 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1998-109885, filed on 2 Jul 1998 Continuation of Ser. No. US 1996-670699, filed on 26 Jun 1996, now patented, Pat. No. US 5820583 Continuation-in-part of Ser. No. WO 1995-US16028, filed on 12 Dec 1995 Continuation-in-part of Ser. No. US 1994-353775, filed on 12 Dec 1994, now abandoned

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Seidel, Richard K.
ASSISTANT EXAMINER:	Thompson, Michael M.
LEGAL REPRESENTATIVE:	Christensen O'Connor Johnson Kindness PLLC
NUMBER OF CLAIMS:	34
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	16 Drawing Figure(s); 12 Drawing Page(s)
LINE COUNT:	3208

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 9 OF 104 USPATFULL

TI Electroporation apparatus with connective electrode template

AB An electrode template apparatus, includes a three dimensional support member having opposite surfaces, a plurality of bores extending through the support member and through the opposite surfaces, a plurality of conductors on the member separately connected to the plurality of bores, a plurality of needle electrodes selectively extendable through the plurality of bores and into tissue to be electroporated so that each electrode is comcected to at least one conductor for connecting the electrodes to a power supply.

ACCESSION NUMBER:	2001:45449 USPATFULL
TITLE:	Electroporation apparatus with connective electrode template
INVENTOR(S):	Hofmann, Gunter A., San Diego, CA, United States

PATENT ASSIGNEE(S): Genetronics, Inc., San Diego, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6208893	B1	20010327
APPLICATION INFO.:	US 1999-234770		19990121 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1998-206635, filed on 7 Dec 1998 Continuation-in-part of Ser. No. US 1998-14291, filed on 27 Jan 1998
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Bockelman, Mark
LEGAL REPRESENTATIVE: Baker & Maxham
NUMBER OF CLAIMS: 30
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 33 Drawing Figure(s); 18 Drawing Page(s)
LINE COUNT: 1328

L7 ANSWER 10 OF 104 USPATFULL
TI Heparin binding peptides
AB The present invention provides heparin antagonist peptides. The heparin-binding peptides of the present invention specifically neutralize heparin's conventional anticoagulant properties without causing deleterious hemodynamic side-effects or exacerbation of the proliferative vascular response to injury. More specifically, the heparin-binding compounds of the present invention are short-duration drugs to be used in elective or emergency situations which can safely and specifically neutralize heparin's conventional anticoagulant properties without causing deleterious hemodynamic side-effects or exacerbation of the proliferative vascular response to injury.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2001:36802 USPATFULL
TITLE: Heparin binding peptides
INVENTOR(S): Harris, Robert B., Midlothian, VA, United States
Sobel, Michael, Syracuse, NY, United States
PATENT ASSIGNEE(S): Commonwealth Biotechnologies, Inc., Richmond, VA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6200955	B1	20010313
APPLICATION INFO.:	US 1998-166930		19981006 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1996-660592, filed on 11 Jun 1996, now patented, Pat. No. US 5877153
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Jones, Dwayne C.
ASSISTANT EXAMINER: Delacroix-Muirheid, Cybille
LEGAL REPRESENTATIVE: Burns, Doane, Swecker & Mathis, L.L.P.
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 23 Drawing Figure(s); 21 Drawing Page(s)
LINE COUNT: 1440
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 11 OF 104 USPATFULL
TI Prevention and treatment of cardiovascular pathologies with tamoxifen analogues
AB A **method** for treating or preventing cardiovascular pathologies by administering a compound of the formula (I): ##STR1##

wherein Z is C.dbd.O or a covalent bond; Y is H or O(C.sub.1 -C.sub.4)alkyl, R.sup.1 and R.sup.2 are individually (C.sub.1 -C.sub.4)alkyl or together with N are a saturated heterocyclic group, R.sup.3 is ethyl or chloroethyl, R.sup.4 is H, R.sup.5 is I, O(C.sub.1 -C.sub.4)alkyl or H and R.sup.6 is I, O(C.sub.1 -C.sub.4)alkyl or H with the proviso that when R.sup.4, R.sup.5, and R.sup.6 are H, R.sup.3 is not ethyl; or a pharmaceutically acceptable salt thereof, effective to elevate the level of TGF-beta to treat and/or prevent conditions such as atherosclerosis, thrombosis, myocardial infarction, and stroke is provided. Useful compounds include idoxifene, toremifene or salts thereof. Further provided is a **method** for identifying an agent that elevates the level of TGF-beta. Another embodiment of the invention is an assay or kit to determine TGF-beta in vitro. Also provided is a therapeutic **method** comprising inhibiting smooth muscle **cell proliferation** associated with procedural vascular trauma employing the administration of tamoxifen or structural analogs thereof, including compounds of formula (I).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2001:33286 USPATFULL			
TITLE:	Prevention and treatment of cardiovascular pathologies with tamoxifen analogues			
INVENTOR(S):	Grainger, David J., Cambridge, United Kingdom Metcalfe, James C., Cambridge, United Kingdom Kunz, Lawrence L., Redmond, WA, United States Schroff, Robert W., Edmonds, WA, United States			
PATENT ASSIGNEE(S):	NeoRx Corporation, Seattle, WA, United States (U.S. corporation)			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6197789	B1	20010306	
	WO 9640098		19961219	
APPLICATION INFO.:	US 1997-973570		19971205	(8)
	WO 1996-US10211		19960607	
			19980908	PCT 371 date
			19980908	PCT 102(e) date
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1995-478936, filed on 7 Jun 1995, now abandoned Continuation-in-part of Ser. No. US 1995-476735, filed on 7 Jun 1995, now patented, Pat. No. US 5595722 Continuation-in-part of Ser. No. US 1995-477393, filed on 7 Jun 1995 Continuation-in-part of Ser. No. US 1995-486334, filed on 7 Jun 1995, now patented, Pat. No. US 5770609			
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Criares, Theodore J.			
LEGAL REPRESENTATIVE:	Schwegman, Lundberg, Woessner & Kluth, P.A.			
NUMBER OF CLAIMS:	17			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 5 Drawing Page(s)			
LINE COUNT:	4577			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

(FILE 'HOME' ENTERED AT 11:41:45 ON 20 JUL 2001)

FILE 'MEDLINE, USPATFULL, HCAPLUS, EMBASE, SCISEARCH, DGENE, WPIDS,

```
     FROSTI, FSTA, CEN, BIOTECHDS, BIOBUSINESS, CEABA-VTB' ENTERED AT
11:42:45
     ON 20 JUL 2001
L1        283229 S CELL PROLIFERATION
L2           788 S L1 AND (REVERSING?)
L3           554 S L2 AND METHOD
L4             0 S CELL PROLIFERATION () REVERSAL () METHOD
L5             0 S CELL PROLIFERATION ADJ REVERSING ADJ METHOD
L6             0 S L3 AND ACTIVATED BLOOD CELLS
L7           104 S L3 AND BLOOD CELLS
L8             0 S L7 AND LACTACYSTIN
L9          1899 S LACTACYSTIN
L10            0 S L9 AND L7
L11           16 S L9 AND RAPAMYCIN
L12            0 S L11 AND L7

=> s l7

L13         104 L7

=> rem dup

DUP IS NOT VALID HERE
The DELETE command is used to remove various items stored by the
system.

To delete a saved query, saved answer set, saved L-number list, SDI
request, batch request, mailing list, or user-defined cluster, format,
or search field, enter the name.  The name may include ?  for left,
right, or simultaneous left and right truncation.

Examples:

  DELETE BIO?/Q           - delete query names starting with BIO
  DELETE ?DRUG/A          - delete answer set names ending with DRUG
  DELETE ?ELEC?/L         - delete L-number lists containing ELEC
  DELETE ANTICOAG/S       - delete SDI request
  DELETE ENZYME/B         - delete batch request
  DELETE .MYCLUSTER       - delete user-defined cluster
  DELETE .MYFORMAT        - delete user-defined display format
  DELETE .MYFIELD         - delete user-defined search field
  DELETE NAMELIST MYLIST - delete mailing list

To delete an ordered document or an offline print, enter its
number.

Examples:

  DELETE P123001C         - delete print request
  DELETE D134002C         - delete document order request

To delete an individual L-number or range of L-numbers, enter the
L-number or L-number range.  You may also enter DELETE LAST followed
by a number, n, to delete the last n L-numbers.  RENUMBER or
NORENUMBER may also be explicitly specified to override the value of
SET RENUMBER.

Examples:

  DELETE L21              - delete a single L-number
  DELETE L3-L6            - delete a range of L-numbers
  DELETE LAST 4           - delete the last 4 L-numbers
  DELETE L33-             - delete L33 and any higher L-number
  DELETE -L55             - delete L55 and any lower L-number
```

```
  DELETE L2-L6 RENUMBER - delete a range of L-numbers and
                          renumber remaining L-numbers
  DELETE RENUMBER       - renumber L-numbers after deletion of
                          intermediate L-numbers
```

Entire sets of saved items, SDI requests, batch requests, user-defined items, or E-numbers can be deleted.

Examples:

```
  DELETE SAVED/Q - delete all saved queries
  DELETE SAVED/A - delete all saved answer sets
  DELETE SAVED/L - delete all saved L-number lists
  DELETE SAVED   - delete all saved queries, answer sets,
                   and L-number lists
  DELETE SAVED/S - delete all SDI requests
  DELETE SAVED/B - delete all batch requests
  DELETE CLUSTER - delete all user-defined clusters
  DELETE FORMAT  - delete all user-defined display formats
  DELETE FIELD   - delete all user-defined search fields
  DELETE SELECT  - delete all E-numbers
  DELETE HISTORY - delete all L-numbers and restart the
                   session at L1
```

To delete an entire multifile SDI request, enter DELETE and the name of the request. To delete a component from the multifile SDI, enter DELETE and the name of the component.

```
=> d his


     (FILE 'HOME' ENTERED AT 11:41:45 ON 20 JUL 2001)

     FILE 'MEDLINE, USPATFULL, HCAPLUS, EMBASE, SCISEARCH, DGENE, WPIDS,
     FROSTI, FSTA, CEN, BIOTECHDS, BIOBUSINESS, CEABA-VTB' ENTERED AT
11:42:45
     ON 20 JUL 2001
L1        283229 S CELL PROLIFERATION
L2           788 S L1 AND (REVERSING?)
L3           554 S L2 AND METHOD
L4             0 S CELL PROLIFERATION () REVERSAL () METHOD
L5             0 S CELL PROLIFERATION ADJ REVERSING ADJ METHOD
L6             0 S L3 AND ACTIVATED BLOOD CELLS
L7           104 S L3 AND BLOOD CELLS
L8             0 S L7 AND LACTACYSTIN
L9          1899 S LACTACYSTIN
L10            0 S L9 AND L7
L11           16 S L9 AND RAPAMYCIN
L12            0 S L11 AND L7
L13          104 S L7

=> d l13 ti abs ibib 90-104


L13  ANSWER 90 OF 104  USPATFULL
TI     Method for ameliorating the adverse effects of aging
AB     Compositions and methods are provided for countering the adverse
effects
       of aging on cells in culture and in vivo in which cells are contacted
       with the compositions that ameliorate the adverse effects of aging on
       mammalian cells by slowing or reversing the changes that
       normally accompanying aging of such cells but do not significantly
       increase the growth rate or total proliferative capacity of such cells.
       The compositions contain one or more 6-(substituted amino)purine
```

cytokinins and preferably do not contain ingredients that promote cell division or that induce or potentiate the ability of the 6-(substituted amino) purine cytokinins to promote cell division.

Among the preferred applications of the compositions and methods provided herein are the preservation of or restoration of the health of mammalian cells in culture and, by application of the compositions to human skin, the health and youthful appearance of the skin.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	97:12477 USPATFULL
TITLE:	**Method** for ameliorating the adverse effects of aging
INVENTOR(S):	Rattan, Suresh I. S., Aarhus V, Denmark
PATENT ASSIGNEE(S):	Senetek PLC, Maryland Heights, MO, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5602139		19970211
APPLICATION INFO.:	US 1994-292721		19940819 (8)

DISCLAIMER DATE:	20111206
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1994-206041, filed on 4 Mar 1994, now patented, Pat. No. US 5371089 which is a continuation of Ser. No. US 1992-954614, filed on 30 Sep 1992, now abandoned which is a continuation-in-part of Ser. No. US 1990-611903, filed on 9 Nov 1990, now abandoned which is a division of Ser. No. US 1987-19150, filed on 26 Feb 1987, now abandoned
DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Jordan, Kimberly
LEGAL REPRESENTATIVE:	Fitch, Even, Tabin & Flannery
NUMBER OF CLAIMS:	4
EXEMPLARY CLAIM:	1
LINE COUNT:	1488

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 91 OF 104 USPATFULL

TI **Method** for identifying an agent which increases TGF-beta levels

AB A **method** for identifying a compound that is a TGF-beta activator or production stimulator is provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	97:5708 USPATFULL
TITLE:	**Method** for identifying an agent which increases TGF-beta levels
INVENTOR(S):	Grainger, David J., Cambridge, England Metcalfe, James C., Cambridge, England
PATENT ASSIGNEE(S):	NeoRx Corporation, Seattle, WA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5595722		19970121
APPLICATION INFO.:	US 1995-476735		19950607 (8)

RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1994-242161, filed on 12 May 1994 which is a continuation-in-part of Ser. No. US 1993-61714, filed on 13 May 1993, now abandoned And Ser. No. US 1994-241844, filed on 12 May 1994 which

is a continuation-in-part of Ser. No. US 1993-62451, filed on 13 May 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-11669, filed on 28 Jan 1993, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Henley, III, Raymond
LEGAL REPRESENTATIVE: Schwegman, Lundberg, Woessner & Kluth, P.A.
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 4090
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 92 OF 104 USPATFULL
TI Methods and compositions for treating thrombocytopenia
AB A **method** and composition utilizing thrombopoietin for increasing platelet cell counts in thrombocytopenia is disclosed. The **method** and composition are suitable for treatments of patients suffering from medical conditions, such as HIV/AIDS or chemotherapy, which result in low platelet cell numbers. Also disclosed are the active moieties or domains of the thrombopoietin molecule.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 97:3518 USPATFULL
TITLE: Methods and compositions for treating thrombocytopenia
INVENTOR(S): McDonald, Ted P., Knoxville, TN, United States
PATENT ASSIGNEE(S): The University of Tennessee Research Corp., Knoxville, TN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5593666		19970114
APPLICATION INFO.:	US 1994-330517		19941027 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1994-291376, filed on 16 Aug 1994, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Weimar, Elizabeth C.
ASSISTANT EXAMINER: Mohamed, Abdel A.
LEGAL REPRESENTATIVE: Daniels, III, John F.
NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Figure(s); 11 Drawing Page(s)
LINE COUNT: 1296
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 93 OF 104 USPATFULL
TI Compounds that inhibit T **cell proliferation** and methods for using the same
AB Compounds which display a surface similar to the surface presented by one of five distinct lateral domains of CD4 are disclosed. Methods of treating individuals suspected of suffering from or susceptible to conditions characterized by an undesired immune response comprising administering to the individual at least one compound which mimics a portion of the lateral surface of the CD4 glycoprotein are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 96:120868 USPATFULL
TITLE: Compounds that inhibit T **cell proliferation** and methods for using the same
INVENTOR(S): Jameson, Bradford A., Philadelphia, PA, United States
McDonnell, James M., Philadelphia, PA, United States

PATENT ASSIGNEE(S): Korngold, Robert, Cherry Hill, NJ, United States
Thomas Jefferson University, Philadelphia, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5589458		19961231
APPLICATION INFO.:	US 1993-76092		19930611 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1992-977692, filed on 13 Nov 1992, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Davenport, Avis M.
LEGAL REPRESENTATIVE: Woodcock, Washburn, Kurtz, Mackiewicz, & Norris
NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1,19
NUMBER OF DRAWINGS: 16 Drawing Figure(s); 15 Drawing Page(s)
LINE COUNT: 1796
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 94 OF 104 USPATFULL
TI Modulation of cellular response to external stimuli
AB The specification discloses methods for modulating cellular metabolism in a subject, modulating being desirable to mitigate a condition of the subject. Disclosed methods include processes for administering to said subject an effective amount of a compound of the formula ##STR1## wherein one and only one of R.sup.1 and R.sup.3 is a straight-chain or branched-chain .omega.-hydroxyalkyl (5-8C), or is a branched-chain (.omega.-1)-hydroxyalkyl (5-8C), or is an (.omega.-1)-oxoalkyl (5-8C), or is an (.omega., .omega.-1) or (.omega.-1, .omega.-2)-dihydroxyalkyl (5-8C), or is an alkenyl substituent (5-8C), and the other is alkyl (1-12C) optionally containing one or two non-adjacent oxygen atoms in place of C.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 96:116387 USPATFULL
TITLE: Modulation of cellular response to external stimuli
INVENTOR(S): Bianco, James A., Seattle, WA, United States
Bursten, Stuart L., Snoqualmie, WA, United States
Singer, Jack W., Seattle, WA, United States
PATENT ASSIGNEE(S): Fred Hutchinson Cancer Research Center, Seattle, WA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5585380		19961217
APPLICATION INFO.:	US 1995-378109		19950125 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1993-155361, filed on 22 Nov 1993, now abandoned which is a division of Ser. No.
US 1992-888722, filed on 26 May 1992, now abandoned which is a continuation-in-part of Ser. No. US 1991-732227, filed on 16 Jul 1991, now abandoned which is a continuation-in-part of Ser. No. US 1991-704992, filed on 24 May 1991, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Gitomer, Ralph J.
LEGAL REPRESENTATIVE: Faciszewski, Stephen
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 27 Drawing Figure(s); 27 Drawing Page(s)
LINE COUNT: 1461
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 95 OF 104 USPATFULL
TI Evaluation and t[redacted]tment of patients with progres[redacted]e immunosuppression
AB A soluble immunosuppressive factor present in ser[redacted] derived from tumor-bearing mammals, is associated with changes in TCR protein subunit levels and T-lymphocyte signal transduction pathway proteins. These changes provide a **method** of determining the level of immunosuppression in a mammal by determining the level of expression of at least one selected TCR subunit protein, or a protein in the T lymphocyte signal transduction pathway, and comparing the level to that found in non-immunosuppressed individuals. The **method** is useful to identify patients having T lymphocytes capable of activation for immunotherapy and for identifying agents which cause or reverse immunosuppression. An isolated immunosuppressive factor associated with the level of expression of the proteins is useful for suppressing the immune response, for example, in organ transplantation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	96:113801 USPATFULL
TITLE:	Evaluation and treatment of patients with progressive immunosuppression
INVENTOR(S):	Ochoa, Augusto C., Washington, DC, United States Mizuguchi, Hiromoto, Frederick, MD, United States O'Shea, John J., Silver Spring, MD, United States Longo, Dan L., Kensington, MD, United States Loeffler, Cynthia M., Pensacola, FL, United States
PATENT ASSIGNEE(S):	Regents of the University of Minnesota, Minneapolis, MN, United States (U.S. corporation) The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5583002		19961210
APPLICATION INFO.:	US 1992-987966		19921211 (7)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1992-863262, filed on 6 Apr 1992, now patented, Pat. No. US 5296353

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Saunders, David
NUMBER OF CLAIMS:	18
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	7 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT:	2252

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 96 OF 104 USPATFULL
TI Evaluation and treatment of patients with progressive immunosuppression
AB A soluble immunosuppressive factor present in serum derived from tumor-bearing mammals, is associated with changes in TCR protein subunit levels, T lymphocyte signal transduction pathway proteins. These changes provide a **method** of determining the level of immunosuppression in a mammal by determining the level of expression of at least one selected TCR subunit protein, a protein in the T lymphocyte signal transduction pathway, or of the NF-.kappa.B/rel family and comparing the level and pattern to that found in non-immunosuppressed individuals. The **method** is useful to identify patients having T lymphocytes

capable of activation for immunotherapy and for identifying agents which cause or reverse immunosuppression. An isolated immunosuppressive factor associated with the level of expression of the proteins is useful for suppressing the immune response, for example, in organ transplantation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	96:85044 USPATFULL
TITLE:	Evaluation and treatment of patients with progressive immunosuppression
INVENTOR(S):	Ochoa, Augusto C., Frederick, MD, United States Longo, Dan L., Kensington, MD, United States Ghosh, Paritosh, Frederick, MD, United States Young, Howard A., Geithersburg, MD, United States
PATENT ASSIGNEE(S):	United States of America as represented by the Secretary of the Department of Health and Human Services, Washington, DC, United States (U.S. government)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5556763		19960917	
APPLICATION INFO.:	US 1993-34832		19930317	(8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-31434, filed on 15 Mar 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-987966, filed on 11 Dec 1992 which is a continuation-in-part of Ser. No. US 1992-863262, filed on 6 Apr 1992, now patented, Pat. No. US 5296353

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Saunders, David
LEGAL REPRESENTATIVE:	Foley & Lardner
NUMBER OF CLAIMS:	11
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	7 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT:	2646

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 97 OF 104 USPATFULL

TI Complexes of nitric oxide with cardiovascular amines as dual acting cardiovascular agents

AB Novel complexes of nitric oxide (NO) and amines are described where the amine is a known cardiovascular agent having at least one or more primary or secondary amino groups and whereby the resulting complex is capable under physiological conditions of releasing in vivo dual active ingredients, the NO and the known cardiovascular agent. The complexes are used for treating cardiovascular diseases and for the prophylactic or therapeutic treatment of restenosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	96:3719 USPATFULL
TITLE:	Complexes of nitric oxide with cardiovascular amines as dual acting cardiovascular agents
INVENTOR(S):	Hutsell, Thomas C., North Oaks, MN, United States
PATENT ASSIGNEE(S):	Comedicus Incorporated, Long Lake, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5482925		19960109	
APPLICATION INFO.:	US 1994-210043		19940317	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Sullivan, Peter
LEGAL REPRESENTATIVE: Merchant, Gould, Smith, Edell, Welter & Schmidt
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
LINE COUNT: 646
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 98 OF 104 USPATFULL
TI Use of delta opioid receptor antagonists to treat immunoregulatory disorders
AB A therapeutic **method** is provided to elevate a depressed mammalian autologous mixed lymphocyte response and to alleviate the diseases associated therewith by the administration of an effective amount of certain selective delta opioid receptor antagonists to a mammal such as a human patient in need of such treatment.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 95:99154 USPATFULL
TITLE: Use of delta opioid receptor antagonists to treat immunoregulatory disorders
INVENTOR(S): Portoghese, Philip S., 17 Oriole La., St. Paul, MN, United States 55127

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